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EXAMINER

SAJJADI, FEREDOUN GHOTB

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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/536,563	Applicant(s) KOKUZAWA ET AL.	
	Examiner Fereydoun G. Sajjadi	Art Unit 1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 22 May 2007.
- 2a) ☒ This action is **FINAL**.                      2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 4-8 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 4-8 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)   | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)                       | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____  |

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## **DETAILED ACTION**

### ***Claim Status***

Applicants' response of May 22, 2007, to the non-final action dated January 25, 2007 has been entered. Claims 4-8 are pending in the application. Claims 4-6 have been amended, and claim 1-3 and 9-14 have been cancelled. No claims were newly added. Claims 4-8 are currently under examination.

Applicants should note that the elected invention (without traverse) is directed to a method of culturing, and proliferating neural stem cells in culture medium comprising HGF, and the elected species of FGF-2. Thus, the examination of the instant claims has been limited to the combination of HGF and FGF-2, there being no allowable generic or linking claim.

### ***Response & New Claim Objections***

Claims 4-6 were objected to for referring to withdrawn claim 1, in the previous office action dated January 25, 2007. In view of Applicants' cancellation of claim 1, the objection is rendered moot and hereby withdrawn.

Claims 4-6 are newly objected to because of the following informalities: the claims have not been amended to recite the elected invention and the species of the invention. The instant claims have been amended to include non-elected subject matter, i.e. HGF and EGF; or HGF, FGF-2 and EGF. Appropriate correction is required.

### ***Claim Rejections - 35 USC § 112- Second Paragraph***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Applicants' claim amendments have necessitated the following new grounds of rejection.

Claims 6-8 are newly rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 6 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. See MPEP § 2172.01. The omitted steps are: culturing neural stem cells under conditions that allow their differentiation into a population of cells containing neurons and glia.

Claims 7-8 depend from claim 6 and have therefore been included in the rejection.

***Response to Claim Rejections - 35 USC § 102***

Claims 4-6 and 8 stand rejected under 35 U.S.C. 102(e) as being anticipated by Csete et al. (U.S. Patent No.: 6,589,728; filed Jan. 31, 2001). The rejections set forth on pp. 2-3 of the previous office action dated January 25, 2007 are maintained for claims 4-6 and 8 for reasons of record.

Applicants traverse the rejection, arguing that Csete et al. do not describe any single growth factor among the long list of growth factors for culturing, proliferating or differentiating neural stem cells, and that Csete et al. disclose that to induce differentiation to neurons and glia, fibroblast growth factor beta (FGFb) is removed from the media; and that Csete et al. are completely silent on any combination of growth factors in the medium, much less the specific combinations of HGF and FGF-2, HGF and EGF, or HGF, FGF-2 and EGF recited in the present methods. Applicants' arguments have been fully considered but are not found persuasive.

In response, it should be noted that FGF-2 and bFGF are synonymous terms for the same growth factor, and that the instant claims have been examined commensurate in scope with the elected invention, i.e. culturing neural stem cells in the presence of HGF and FGF-2.

As indicated in the previous office action, Csete et al. teach a method for isolating, maintaining, enriching and differentiating stem or precursor central nervous system cells from fetal rat brain, that are dissociated to a single-cell suspension and plated on tissue culture dishes in medium containing bFGF. Further teaching that the medium for isolation, proliferation and differentiation of the stem cells may be supplemented with a variety of growth factors, cytokines and serum, that include hepatocytes growth factor (HGF) (column 7). Thus teaching all the limitations of instant claims 4-6 and 8.

It is additionally noted that instant claims 4 and 5 are directed to methods of culturing and proliferating neural stem cells and not differentiation. Further, while the preamble of claim 6

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recites a method of differentiating neural stem cells, the method step recited in the claim is directed to culturing neural stem cells in a growth medium comprising HGF and FGF-2, and not to differentiation of said cells. None the less, Csete et al. teach that the medium for proliferating the stem cells and the medium for differentiation of these cells can be the same or different (lines 42-45; column 7).

Therefore the rejection is maintained for claims 4-6 and 8 for reasons of record and the foregoing discussion.

***Response to Claim Rejections - 35 USC § 103***

Claim 7 stands rejected under 35 U.S.C. §103(a) as being unpatentable over Csete et al. (U.S. Patent No.: 6,589,728; filed Jan. 31, 2001), in view of Luskin (U.S. Patent No.: 5,753,505; filed Jul. 6, 1995). The rejections set for the on pp. 3-4 of the previous office action dated January 25, 2007 are maintained for claims 4-6 and 8 for reasons of record.

Applicants traverse the rejection, arguing that the combined disclosures of Csete and Luskin do not disclose or suggest all of the limitations of the claims, because Csete does not disclose or suggest including any combination of growth factors in the medium, much less the specific combinations of HGF and FGF-2, HGF and EGF, or HGF, FGF-2 and EGF recited in the present methods, and that Luskin does not supply the elements missing from Csete. Applicants' arguments have been fully considered but are not found persuasive.

It should again be noted that that the instant claims have been examined commensurate in scope with the elected invention, i.e. culturing neural stem cells in the presence of HGF and FGF-2. Applicants' are directed to the response set forth above regarding the teachings of Csete et al.

Applicants further argue that the results shown in Figure 1 (b) and Table 1 with respect to culture and the proliferation of neurospheres cultured in growth medium in the presence of HGF and FGF-2 constitute unexpected and superior results of the present method (3100 versus 900 for culture in HGF alone). Such is not found persuasive, because it is not clear why an increase in proliferative capacity of the cells in the presence of growth factors additional to HGF alone would be considered unexpected. HGF and FGF2 are structurally and functionally distinct

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growth factors and the use of combinations of growth factors in enhancing the proliferative potential of cells in culture was well known in the art as demonstrated by the teachings of Csete et al. Moreover, any "unexpected" results would be so considered in view of an expected result. In the instant case, the expected result is an increased proliferative potential when more than one growth factor is utilized in a culture medium.

As indicated in MPEP 716.02(c), "Expected beneficial results are evidence of obviousness of a claimed invention, just as unexpected results are evidence of unobviousness thereof." *In re Gershon*, 372 F.2d 535, 538, 152 USPQ 602, 604 (CCPA 1967).

Therefore the rejection of claim 7 is maintained for reasons of record and the foregoing discussion.

### ***Conclusion***

#### **Claims 4-8 are not allowed.**

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. The claims are drawn to the same invention claimed earlier in the application and would have been finally rejected on the grounds and art of record in the next Office Action if they had been entered earlier in the application. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire **THREE MONTHS** from the mailing date of this action. In the event a first reply is filed within **TWO MONTHS** of the mailing date of this final action and the advisory action is not mailed until after the end of the **THREE-MONTH** shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than **SIX MONTHS** from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Fereydoun G. Sajjadi whose telephone number is (571) 272-3311. The examiner can normally be reached on 7:00-4:00.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989).

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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